

**Primary Carcinosarcoma of the Ovary: A Report of 3 Cases**  
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**ABSTRACT**

We aim to present three cases of carcinosarcoma of the ovary, rare tumor associated with an aggressive clinical course and overall poor prognosis. Ovarian carcinosarcoma is a rare gynecologic malignancy that tends to develop in elderly women. These tumors are defined histologically by the presence of malignant epithelial and stromal elements. They are associated with a poor prognosis. The optimal chemotherapeutic regimen to treat this tumor is yet to be determined. The ages of patients were 56, 62, 58 years. Three patients underwent a primary debulking surgery, and adjuvant chemotherapy. After surgery the pathologic examination reported a primary ovarian carcinosarcoma.

**Keywords:** Carcinosarcoma, mmalign mixed mullarian tumor, ovary

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## **INTRODUCTION**

Malign mixed mullerian tumors (MMMTs) of the ovary is a rare tumor with a poor prognosis that comprises 1–4% of all ovarian malignancies (1-4). These tumors are histologically defined by the presence of malignant epithelial and stromal elements which may be either homologous (composed of tissues normally found in the ovary) or heterologous (containing tissues not normally found in the ovary). Examples of homologous sarcomatous components include endometrial stromal sarcoma, fibrosarcoma and leiomyosarcoma. Examples of heterologous sarcomatous elements include chondrosarcoma, rhabdomyosarcoma, and less frequently, osteosarcoma or liposarcoma. The epithelial component is often classified as serous, endometrioid or undifferentiated adenocarcinoma but may also represent clear cell adenocarcinoma or squamous cell carcinoma. According to the National Comprehensive Cancer Network clinical practice guidelines in oncology (2008), MMMTs is classified as a carcinosarcoma. They most commonly are identified in the uterus. Carcinosarcoma of the ovary has a worse survival rate when compared to epithelial ovarian cancers (1,4,5), with a median survival of <18 months. Omentectomy and complete debulking surgery followed by platinum-taxane based chemotherapy is the treatment of choice for this type of malignancy. We report three of patients with carcinosarcoma of the ovary, outlining the clinical features, pathologic characteristic, and management.

### **Case 1**

A 58-year-old female presented with right lower abdominal pain and a pelvic mass. The woman, gravida 3, para 2, who went through menopause at 45 years of age, with no history of hormone therapy. Ultrasonography revealed a large right adnexal solid mass. Laboratory test results were generally within normal limits. Tumor markers

revealed the carcinoembryonic antigen was 2.05 ng/mL, cancer antigen (CA) 125 was 182 U/mL. The patient underwent exploratory laparotomy, and right ovarian tumor with abdominal carcinomatosis were noted. The tumor involved the uterine surface, cul-de sac, pelvic wall, intestinal wall, mesentery and omentum. Frozen test proved that the mass was malignant. Patient underwent total hysterectomy with bilateral salpingo-oophorectomy and partial omentectomy. The ovarian tumor was measuring 20x15x10 cm.

It was solid mass with necrosis and hemorrhaging. The left ovary appeared normal. Histopathological examination of the tumor showed a picture consistent with the heterologous variety MMT composed of an epithelial element and a mesenchymal element. The epithelial element was composed of endometrioid carcinoma, and the mesenchymal element was composed of rhabdomyosarcoma (Figure 1). The epithelial element was immunoreactive for cytokeratin, the mesenchymal element was immunoreactive for desmin. Final diagnosis of primary heterologous ovarian MMT stage IIIc was given. Following the debulking surgery, adjuvant chemotherapy was administered as carboplatin and taxol. The patient died from her disease after 24 months.

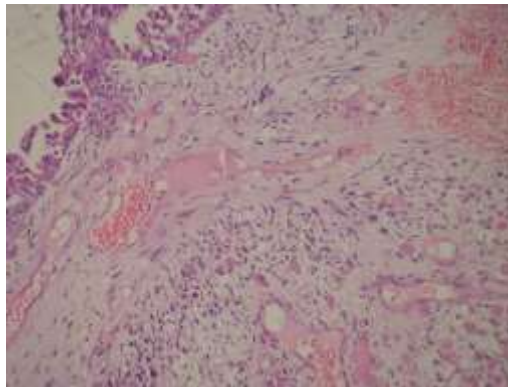


Figure 1: Endometrioid adenocarcinoma and rhabdomyosarcoma

## Case 2

A 62-year-old, gravida 4, para 2, post-menopausal woman, with abdominal pain, showed a large pelvic mass. The woman with history of hormone therapy during four years. Physical examination revealed a huge pelvic mass. Transvaginal ultrasound was performed showing left pelvic mass approximately 120x98x80 mm in size, with flow and solid components. Ultrasound showed an ovarian mass with both solid and cystic areas. A total abdominal hysterectomy with bilateral salpingo-oophorectomy and totally omentectomy were performed. Frozen section of the specimen was reported as malignant. The left ovary was 12x8x7 cm and had a disordered contour. The capsule was not intact, showing infiltration. The cut surface was yellow, white and hemorrhagic areas were seen. Histologically biphasic differentiation of the tumor was present in most of the fields sampled. Epithelial element was high grade serous carcinoma. The stromal component showed a highly cellular neoplasm composed of spindle-shaped with hyperchromasia and pleomorphism (Figure 2).

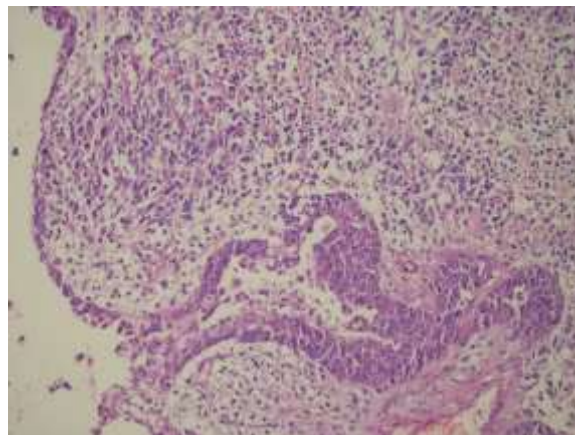


Figure 2: Serous carcinoma and sarcomatous component

No heterologous components could be identified. Immunohistochemical study showed positive staining in the epithelial neoplastic cells with cytokeratin, p53 and the mesenchymal element with desmin. The final pathology was reported as MMMT stage IIIa of the ovary. The patient was given adjuvant carboplatin-taxol based chemotherapy after the surgery. Follow-up after completion of therapy showed in the tumor marker, and the computed tomography scan did not disclose recurrence.

### **Case 3**

A 56-year-old parous woman was admitted to our hospital with a complaint of abdominopelvic pain and vaginal bleeding. On abdominopelvic examination, a solid, irregular surface was noticed in the right lower quadrant. Serum CA 125 was 29,5 U/mL and other tumor markers were normal limits. On transvaginal ultrasonography, a solid and cystic heterogeneous tumor with a diameter of 120x110x80 mm was revealed on the right ovary. Total hysterectomy, bilateral salpingo-oophorectomy, and omentectomy were performed. The operative specimens of this patient included the right ovarian tumor was a 12 cm solid-necrotic neoplasm. Frozen section of the tumor was reported as malignant. The right ovary was 12x10x8 cm and had a well-circumscribed contour. The capsule was intact. Sections showed cystic areas containing soft yellow, as well as solid areas with hemorrhage and necrosis. Hematoxylin and eosin stained sections from the solid area showed a malignant tumor with two distinct components (Figure 3).

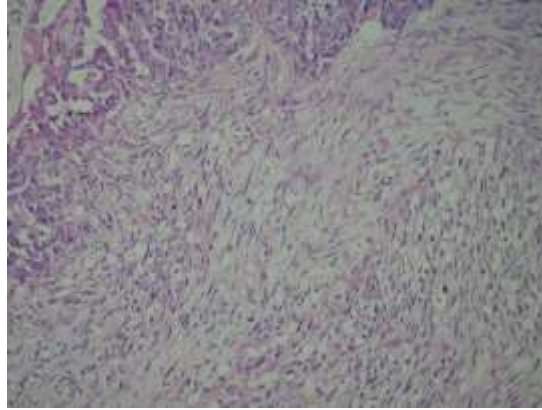


Figure 3: Serous carcinoma and spindle cell sarcoma

One of the components was epithelial showing high grade serous carcinoma. There was nuclear anaplasia and atypical mitosis. The other component revealed features of pleomorphic spindle cell sarcoma with marked pleomorphism and hyperchromasia frequent mitoses and necrosis. The mesenchymal element was composed of rhabdomyosarcoma. The epithelial and mesenchymal components were closely intermixed without well-demarcated boundaries. On immunohistochemistry, the malignant epithelial cells were reactive for high molecular weight keratin while the pleomorphic spindle cell sarcomatous component showed diffuse positivity for vimentin and desmin. The final pathology was reported as carcinosarcoma of the ovary. After the pathologic diagnosis, the patient was given adjuvant carboplatin-taxol based chemotherapy. The patient was followed with serum tumor marker CA 125 and imaging studies, i.e., computed tomography. The patient is alive without evidence of disease at the time of the last follow-up.

## DISCUSSION

Ovarian carcinosarcoma is a rare, highly aggressive tumor with extremely unfavorable prognosis and a biphasic neoplasm with malignant epithelial and malignant mesenchymal elements. This type of tumor is unusual and only a few cases are reported each year. The main differential diagnosis in cases of MMMTs includes sarcomatoid carcinoma and immature teratoma. In 6 sarcomatoid carcinoma, the carcinomatous elements blend with the sarcomatoid component, unlike the sharply demarcated components seen in cases of MMMT. Immature teratoma is somewhat difficult to distinguish, as both tumors may contain elements derived from all three germ cell layers; neuroectodermal tissue, however, has only rarely been reported in MMMTs. These two tumors also occur in different age groups; immature teratomas show a peak in childhood and in young adulthood, while MMMTs occur in the postmenopausal setting. The most common symptoms of carcinosarcoma of the ovary are abdominal pain and abdominal mass. Ca 125 is highly specific marker for ovarian tumors, and it has also been shown to be a useful tumor marker for ovarian carcinosarcoma. Diverse outcomes are seen in the literature with some reports demonstrating a dismal 7–10 month survival (6,7) and others reporting more favorable outcomes with 16–27 month survival (8-10). Ozguroglu et al. have reported that one of the best predictors to response is the histological pattern. Predominating carcinomatous or sarcomatous component should be taken into consideration in predicting the response and planning the chemotherapy protocol (11). Sood et al. showed that patients with cancers with homologous sarcomatous elements had a significantly better survival compared to those with cancers containing heterologous elements (9). But recent studies have suggested that there was no correlation and currently sarcomatous type is not considered a prognostic factor. On the other hand,

serous epithelial components have been proven to be associated with a worse survival compared to nonserous epithelial components. Duman et al. have thought that the ratio of sarcomatous and carcinomatous components in these tumors can be predictor of treatment choice (12). In the literature, clinical prognostic factors associated with poor survival have included advanced stage at presentation, suboptimal debulking and older age. The stage was the most significant prognostic factor in ovarian MMT's (13). Barakat et al. demonstrated a median survival of 104.8 months in patients with stage I or II disease compared to 9.5 months in patients with stage III or IV disease (11). Barnholtz-Sloan et al. reported, the median survival of women with early-stage ovarian MMT was 64 months and for advanced-stage ovarian MMT was 13 months (4). Treatment for advanced disease consists of complete surgical staging and debulking and postoperative adjuvant chemotherapy. Because of the rare occurrence of these tumors, with fewer than 500 cases reported in the English literature (5), no consensus has emerged yet as to what constitutes the most effective chemotherapy. Common treatment combinations utilized to date include platinum and/or paclitaxel and platinum and/or ifosfamide. The combination of paclitaxel and carboplatin has been an effective regimen for epithelial ovarian cancers; physicians have hypothesized that the regimen would also be effective for treatment of ovarian carcinosarcomas. According to large retrospective series (4,5,6), the optimal treatment for malignant mixed mullerian tumors of the ovary consists of cytoreductive surgery followed by platinum-based chemotherapy. The Gynecologic Oncology Group (GOC) has undertaken several prospective studies of chemotherapy for women with ovarian carcinosarcoma. Although limited by small sample size, an analysis of 22 patients treated with either carboplatin and paclitaxel or cisplatin and ifosfamide found no difference in survival (14). Rutledge et al. reviewed the literature for response rate of platinum based



chemotherapy compared to non-platinum based regimens and reported response rates of 68%. Duska et al. noted on 28 cases treated with platinum and taxane who had a total response rate of 72%. Leiser and co-workers showed in a cohort study of 30 cases with ovarian carcinosarcoma treated with platinum and taxane, response rate of %63, and Rauh-Hain et al. noted a response rate of 62% (5). Ifosfamide has also been studied in MMT of the ovary and ifosfamide could be used as second line therapy after platinum-based chemotherapy in some reports. Also, ifosfamide is often associated with substantial toxicity and hospital-requiring portion of the treatment. For this reason further work is needed to examine the patterns of ifosfamide chemotherapy use in women with MMT. However, radiotherapy may be appropriate for patients with chemotherapy-refractory recurrent or persistent disease that is restricted to the pelvis. Invariably, a diagnosis of advanced stage carcinosarcomais associated with a dismal prognosis, and most studies record few survivors at 2 years or even 1 year.

We report three cases of primary carcinosarcoma of the ovary with advanced diseases. After optimal debulking surgery, combination chemotherapies with carboplatin-taxol were given. In conclusion, patients with carcinosarcoma of the ovary have a low response to chemotherapy and worse survival. Aggressive surgical treatment may play a role. However, further alternative systemic therapeutic studies and the different agents for the treatment of carcinosarcoma are required.

Disclosure Statement: The authors declare that they have no conflict interest.

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